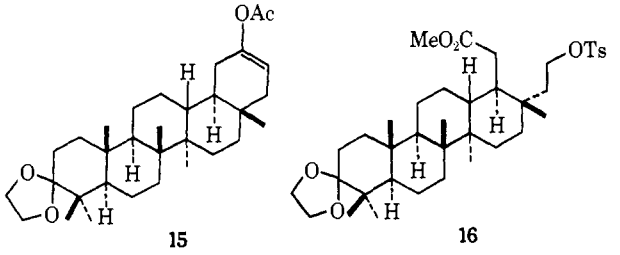
The resulting pentacyclic ketol **14**, mp 269–271° (*m/e* 414.3493), differs from our goal, the ester **2**, only in ring E. We now describe the steps which served to transform **14** into **2**. Ketalization of **14** gave the dioxolane alcohol, mp 188–190°, oxidized to the ring E ketone, mp 230–232°, which was smoothly converted to its enol acetate **15**, mp 198–199°, by quenching the enolate (2.5-hr reflux with excess sodium hexamethyldisalazane in tetrahydrofuran) with acetic anhydride. Ozonolysis of **15** (methylene chloride–methanol (2:1), −70°, followed by sodium borohydride–sodium hydroxide at 0°), acidification (10% acetic acid), esterification (diazomethane), and tosylation led to the isolation of the crude tosylate ester **16** (silica gel–benzene ether, 10:1) which we expected to cyclize readily to the (±)-pentacyclic ketal ester **2**. This proved to be the case. Upon heating for 30 min with an excess of sodium hexamethyldisilazane in benzene, cyclization of **16** gave an 80% yield of (±)-**2**, mp 200–202° from ether–hexane. (*Anal.* Found: C, 76.31; H, 10.39). The ir, nmr, and mass spectra of (±)-**2** were identical with those of the methyl ester **2** derived from natural lupeol (*vide supra*).[11]



15 **16**

Since the path from **2** to lupeol had already been delineated (*vide supra*) the route was now complete between β-naphthol (the precursor of our starting material, the tricyclic enone **3**) and lupeol.

Acknowledgments. We wish to thank the National Science Foundation and the National Institutes of Health for the support of this work.

(11) Although formally unnecessary, we also converted our (±)-2 to (±)-lupeol, but because of the small scale on which we carried out this transformation, the melting point (202–204°) of our material may be low.

Gilbert Stork,* Shoichiro Uyeo
T. Wakamatsu, P. Grieco, J. Labovitz
Department of Chemistry, Columbia University
New York, New York 10027
Received June 26, 1971

Determination of Various Hydrogen–Deuterium Isotope Effects in Carbanion Reactions Using Electron Transfer as a Reference Reaction

Sir:

We wish to report a convenient method for measuring isotope effects on carbanion protonation at steady-state concentrations and to draw some general conclusions regarding such reactions. It has been suggested[1] that observation of a substantial hydrogen isotope effect on the ionization of a carbon acid requires that the protonation of the resultant carbanion show a similar isotope effect and that this is only possible in cases where the reprotonation is not diffusion controlled. Other approaches to the assessment of reprotonation rates include the association of linear Brønsted plots of log k (isotopic exchange) *vs.* pK_a[2] and the occurrence of internal return[3] with diffusion-controlled reprotonation.

Experimentally, the situation is highly contradictory. Substituted triphenylmethane systems in *tert*-butyl alcohol show both internal return[4,5] and primary isotope effects.[6] Substituted fluorenes in methanol not only exhibit isotope effects[7] and internal return[8] but also give linear Brønsted plots.[9]

Electron-transfer trapping of such carbanions[10] adds a new dimension to the problem and, in our opinion, demonstrates a relatively slow reprotonation for those anions which can be trapped. This category has previously been shown to include potassium triphenylmethide in *tert*-butyl alcohol[10] and in this paper is extended to 9-methoxyfluorenide ion in methanol. Electron transfer trapping can also be used to demonstrate isotope effects. We have determined not only the primary isotope effect for proton removal from the carbon acid, following the method of Russell,[11] but have extended the technique to determination of solvent isotope effects. Most importantly, we have been able to measure the primary isotope effect for proton removal by the carbanion from solvent molecules. The data on which these determinations are based are listed in Table I. These results can be analyzed in terms of

Table I. Rate Constants for Exchange and Loss of 9-Methoxyfluorene Catalyzed by Potassium Methoxide (0.47 *N*) in Methanol at 30.0°

Run	Substrate	Solvent	Acceptor[c]	k_{ex},[a] M^{-1} sec^{-1}	k_{loss},[b] M^{-1} sec^{-1}
1	RH	MeOD	None	5.97×10^{-4}	
2	RH	MeOD	3,5-$Cl_2C_6H_3NO_2$		6.12×10^{-4}
3	RD	MeOH	None	4.40×10^{-5}	
4	RD	MeOH	3,5-$Cl_2C_6H_3NO_2$		4.45×10^{-5}
5	RH	MeOH	3,5-$Cl_2C_6H_3NO_2$		2.53×10^{-4}
6	RH	MeOH	$C_6H_5NO_2$		1.22×10^{-5}
7	RD	MeOD	3,5-$Cl_2C_6H_3NO_2$		1.15×10^{-4}
8	RD	MeOD	$C_6H_5NO_2$		2.41×10^{-5}

[a] Exchange was followed by isolation of substrate and mass spectral analysis. At least five points were taken per kinetic run and rate constants determined by the least-squares method. The correlation coefficient was greater than 0.99 and reproducibility in duplicate runs was within 2%. [b] Loss was followed by gas chromatography, relating unreacted substrate to internal hexadecane. Excellent first-order kinetics were again obtained with reproducibility within 3%. The product of the reaction was almost exclusively (80% recovery) 9,9′-dimethoxy-9,9′-bifluorene from deoxygenated reaction mixtures under purified nitrogen. This is indisputably the product of an electron transfer reaction. Unreacted substrate in run 2 contained no D. [c] 0.2 *M*.

(1) G. A. Russell, A. G. Bemis, E. J. Geels, E. G. Janzen, and A. J. Moye, *Advan. Chem. Ser.*, No. 75, 174 (1968).

(2) D. J. Cram in "Fundamentals of Carbanion Chemistry," A. T. Blomquist, Ed., Academic Press, New York, N. Y., 1965, p 14.

(3) C. D. Ritchie and R. E. Uschold, *J. Amer. Chem. Soc.*, 90, 2821 (1968).

(4) D. J. Cram, F. Wiley, H. P. Fischer, and D. A. Scott, *ibid.*, **86**, 5370 (1964).

(5) R. D. Guthrie and G. R. Weisman, *Chem. Commun.*, 1316 (1969).

(6) R. D. Guthrie, *J. Amer. Chem. Soc.*, **92**, 7219 (1970).

(7) A. Streitwieser, Jr., and F. Mares, *ibid.*, **90**, 2444 (1968).

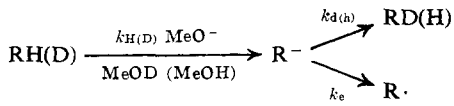
(8) W. T. Ford, E. W. Graham, and D. J. Cram, *ibid.*, **89**, 689 (1967). The authors observe about 5% isoinversion. Isoretention, an invisible process, might well be larger.

(9) A. Streitwieser, J. I. Brauman, J. H. Hammons, and A. H. Pudjaatmaka, *ibid.*, **87**, 386 (1965).

(10) R. D. Guthrie, *ibid.*, **91**, 6201 (1969).

(11) G. A. Russell and A. G. Bemis, *ibid.*, **88**, 5491 (1966).

the illustrated reaction scheme.



Within experimental error, $k_1 = k_2$ (subscripts are run numbers) and $k_3 = k_4$, demonstrating that in runs 2 and 4 the reaction is ionization limited. Moderate changes in acceptor concentration produced no change in rate constant, supporting this conclusion. Because $k_5 = k_H$ and $k_4 = k_D$, the primary isotope effect is $k_5/k_4 = k_H/k_D = 5.7$ (in MeOH). Similarly, $k_2/k_7 = k_H/k_D = 5.3$ (in MeOD). Solvent isotope effects are $k_2/k_5 = k_{H(MeOD)}/k_{H(MeOH)} = 2.4$ and $k_7/k_4 = k_{D(MeOD)}/k_{D(MeOH)} = 2.6$.

The isotope effect for carbanion protonation is calculated as follows: for loss of RH in MeOH, $k_6 = k_{H(MeOH)}k_e/(k_e + k_h)$ and $k_5/k_6 = (k_e + k_h)/k_e$, giving $k_h/k_e = 19.7$. The same method gives $k_d/k_e = 3.7$, and, therefore, $k_h/k_d = 5.3$. (A value of 5.2 was obtained at 0.81 *N* KOMe.) If microscopic reversibility is assumed, two conclusions are suggested: first that the change from H to D produces about the same change in zero-point energy for OH in methanol as for CH in 9-methoxyfluorene and second that the change in solvent (MeOH *vs.* MeOD) does not affect the electron-transfer rate. These conclusions are not independent; rather the assumption of one requires the other and the incorrectness of one requires a fortuitously compensating incorrectness in the other.

If both k_H and k_D are measured in the same solvent, $k_H/k_D \cong 5.5$. If k_H and k_D are measured in isotopically different solvents, k_H/k_D is modified by the solvent isotope effect, for example, $k_{H(\text{in MeOH})}/k_{D(\text{in MeOD})} = k_5/k_7 = 2.2$. This shows that the isotopic nature of the medium affects the free-energy difference between the starting state (RH(D) and MeO⁻) and the transition state in a manner independent of covalent bond-breaking processes. As the free-energy difference between the product state (R⁻ and MeOH(D)) and the transition state is affected by the isotopic nature of the medium only to that extent expected for the primary, bond-breaking isotope effect ($k_{h(MeOH)}/k_{d(MeOD)} = 5.3$), it may be inferred that the product state and the transition state are similarly solvated, whereas the starting state, in particular methoxide ion, must be appreciably desolvated enroute to the transition state.

It should be made clear that the reverse isotope effect measured in this manner does not necessarily indicate that the carbanion would select MeOH molecules in preference to MeOD molecules if exposed to a mixture of both. We have merely demonstrated a longer lifetime[12] for 9-methoxyfluorenide ion in the deuterated solvent. Although this could result from a greater fraction of productive encounters in MeOH *vs.* MeOD, it could also indicate a situation in which all encounters lead to protonation but where the average time between encounter and protonation is greater in MeOD. This point deserves further study in that the latter alternative could allow the occurrence of intramolecular reprotonation even in the case of trappable anions.

(12) Although we can determine only relative lifetimes, reprotonation of the carbanion must be well below the diffusion-controlled limit. Ionization is rate limiting for the electron-transfer reaction at concentrations of 3,5-dichloronitrobenzene down to 0.05 *M*. Stoichiometric studies show clearly that complexation between the reagents and the acceptor is not important and that the acceptor is therefore acting as a true bimolecular interceptor for the anion.

Acknowledgment. We wish to thank the National Science Foundation for a grant (GP-17465) supporting this work.

Robert D. Guthrie,* A. T. Young, G. W. Pendygraft
Department of Chemistry, University of Kentucky
Lexington, Kentucky 40506
Received May 27, 1971

Reaction of Methylenecyclopropanes with Tetracyanoethylene. A New Cycloaddition Involving Three- and Two-Carbon Units

Sir:

Most thermal [2 + 2 + 2] cycloadditions[1] hitherto presented are viewed as involving either a symmetry-allowed [$_\pi 4_s$ + $_\pi 2_s$] process (Diels–Alder reaction)[2] or a [$_\pi 2$ + $_\pi 2$ + $_\pi 2$] reaction.[3] Comparatively few examples are known of the intermolecular [$_\sigma 2$ + $_\pi 2$ + $_\pi 2$] cycloaddition where a C–C single bond participates as a two-electron component.[4,5] This paper describes a thermal cycloaddition of methylenecyclopropanes to tetracyanoethylene (TCNE) which, at least formally, falls into this category, and the substituent dependency of the reaction mode.

When a mixture of 2-phenyl-1-methylenecyclopropane (**1a**) and TCNE (1:1.2 mole ratio) in benzene was heated at 100° for 5 days under nitrogen atmosphere, five-membered cycloadducts, **2a** [mp 151–152°; uv (C_2H_5OH) λ_{max} 261 (log ϵ 4.26) and 293 nm (shoulder); nmr ($CDCl_3$, TMS) δ 3.63 (broad s, 4 H, CH_2), 6.78 (m, 1 H, =C*H*C_6H_5), and 7.37 (m, 5 H, C_6H_5)] and **3a** [mp 97.5–98.5°; nmr ($CDCl_3$) δ 3.68 (m, 2 H, CH_2), 4.65 (m, 1 H, C*H*C_6H_5), 5.29 and 5.62 (m, 1 H each, =CH_2), and 7.48 (s, 5 H, C_6H_5)][6,7] were obtained in 40 and 25% yields, respectively (eq 1). Similarly, reaction of 2,2-diphenyl-1-methylenecyclopropane (**1b**) and TCNE (100°, 3 days) gave **2b** (45%) [mp 142.5–143.5°; uv (C_2H_5OH) λ_{max} 260 nm (log ϵ 4.07); nmr ($CDCl_3$) δ 3.51 (s, 4 H, CH_2) and 7.35 (m, 10 H, C_6H_5)] and **3b**

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(4) For possible [$_\sigma 2$ + $_\pi 2$ + $_\pi 2$] cycloadditions previously reported: (a) S. Sarel and E. Breuer, *ibid.*, **81**, 6522 (1959); (b) F. W. Fowler, *Angew. Chem., Int. Ed. Engl.*, **10**, 135 (1971); (c) J. E. Baldwin and R. K. Pinschmidt, Jr., *Tetrahedron Lett.*, 935 (1971).

(5) For the [$_\sigma 2_a$ + $_\sigma 2_a$ + $_\pi 2_s$] cycloaddition, see C. D. Smith, *J. Amer. Chem. Soc.*, **88**, 4273 (1966).

(6) All new compounds gave correct elemental analyses and consistent spectral data (ir, uv, nmr, and mass spectra). The authors thank Professor A. Tatematsu, Meijo University, for measurement of the high-resolution mass spectra.

(7) Careful ozonolysis of **2a** at −78° followed by reductive work-up[8] gave 3,3,4,4-tetracyanocyclopentanone [mp 127–129° dec; ir (KBr) 2240 (CN) and 1778 cm⁻¹ (C=O)][6] and benzaldehyde, whereas **3a** was converted into 3,4,4-tricyano-2-phenylcyclopentenone [mp 161.5–163.5° dec; ir (KBr) 2240, 2220 (CN), and 1745 cm⁻¹ (C=O)].[6]

(8) J. J. Pappas, W. P. Keaveney, E. Gancher, and M. Berger, *Tetrahedron Lett.*, 4273 (1966).